

Models

Components
IV Models
Absorption Models
Covariates

Bioequivalence

A Case Example

Introduction to mrgsolve : Hands on tutorial

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Presentation Overview

Models

Components
IV Models
Absorption Models
Covariates

Bioequivalence

A Case Example

- 1 Models
 - Components
 - IV Models
 - Absorption Models
 - Covariates
- 2 Bioequivalence
 - A Case Example

Models

Components

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Components

Minimum Components

Closed-form

- \$PROB
- \$GLOBAL
- \$PKMODEL
- \$CMT
- \$PARAM
- \$CAPTURE

ODEs

- \$PROB
- \$GLOBAL
- \$CMT
- \$PARAM
- \$ODE
- \$CAPTURE

Models

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A Case Example

```

1 $PROB
2 #one compmt model (IV
   administration)
3
4 $GLOBAL
5 #define CP (CENT/V)
6
7 $PKMODEL ncmt = 1, depot =
   FALSE
8
9 $PARAM @annotated
10 CL    : 1 : Clearance (
   volume/time)
11 V     : 20 : Central volume
   (volume)

```

IV Models

Closed-form

```

1
2 $CMT @annotated
3 CENT    : Central
   compartment (mass)
4
5 $CAPTURE @annotated
6 CP      : Plasma concentration
   (mass/time)

```

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A Case Example

```

1 $PROB
2 #one compt model (IV
   administration)
3 $GLOBAL
4 #define CP (CENT/V)
5
6 $CMT @annotated
7 CENT : Central compartment
8
9 $PARAM @annotated
10 CL   : 1 : Clearance (
      volume/time)
11 V    : 20 : Central volume
      (volume)

```

IV Models
ODEs

```

1
2 $ODE
3 dxdt_CENT = - CL*CP;
4
5 $CAPTURE @annotated
6 CP : Plasma concentration
      (mass/volume)
7
8

```

Absorption Models

Closed-form

Models

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A Case Example

```

1 $PROB
2 #one compt model with
   first order absorption
3
4 $GLOBAL
5 #define CP (CENT/V)
6
7 $PKMODEL ncmt = 1, depot =
   TRUE
8
9 $CMT @annotated
10 EV : Extravascular
   compartment
11 CENT : Central compartment

```

```

1 $PARAM @annotated
2 CL : 1 : Clearance (
   volume/time)
3 V : 20 : Central volume
   (volume)
4 KA : 1 : Absorption
   rate constant (1/time)
5
6 $CAPTURE @annotated
7 CP : Plasma concentration
   (mass/volume)
8
9

```

Absorption Models

ODEs

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A Case Example

```

1 $PROB
2 #one compt model with
   first order absorption
3 $GLOBAL
4 #define CP (CENT/V)
5
6 $CMT @annotated
7 EV   : Extravascular
       compartment
8 CENT : Central compartment
9
10
11 $PARAM @annotated
12 CL   : 1 : Clearance (
       volume/time)
13 V    : 20 : Central volume
       (volume)
14 KA   : 1 : Absorption
       rate constant (1/time)

```

```

1
2
3 $ODE
4 dxdt_EV = -KA*EV;
5 dxdt_CENT = KA*EV - CL*CP
   ;
6
7 $CAPTURE @annotated
8 CP : Plasma concentration
     (mass/volume)
9
10

```

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Covariates

Covariates

- Covariates must be defined under \$MAIN and \$PARAM

```

1 [PARAM] @annotated
2 WT      : 70 : Weight (kg)
3 CLCR    : 83 : Creatinine
              clearance (ml/min)
4 AGE     : 35 : Age (years)
5
6 [MAIN]
7
8 double TVCL      = THETA1;
9 double CL_AGE    = THETA5;
10 double CL_CLCR   = THETA9;

```

```

1
2 double LOGTWT = 0.75*log((
              WT/70.0));
3 double LOGTAG = log((AGE/
              35.0));
4 double LOGTCLCR = log((
              CLCR/83.0));
5 double CL = exp(log(TVCL)
              + CL_AGE * LOGTAG +
              CL_CLCR * LOGTCLCR +
              LOGTWT + ETA(1)) ;

```


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BE.R

- Calculate NCA param using PKNCA library
- Forest plots with pmForest
- Use lme library for BE calculation

To do

- Build the mrgsolve model for 2 cmpt with first order absorption
- simulate salt QD vs base TID
- calculate AUC over 24 hrs